AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1-36 (cancelled).

37. (currently amended) A method of using a computer for selecting at least one of a plurality of chemical entities based on its ability to associate with all or part of a molecule or molecular complex comprising a calcineurin A (CnA) binding pocket defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 150, 151, 156, 160, 199, 232, 253, 254, 256, 281, 282, 283, 284, 306, 311, 312, and 317 according to Figure 1~~, or a CnA homologue binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å~~;

wherein said computer comprises a machine-readable data storage medium comprising a data storage material encoded with said structure coordinates ~~defining all or part of said binding pocket~~ and wherein said method comprises the steps of:

a) producing a crystal of a molecule or molecular complex comprising amino acids [[5-168]] 24-240 and 247-370 of CnA and amino acids [[24-370]] 5-82 and 84-168 of CnB and a chemical entity;

b) determining the three-dimensional structure coordinates of the molecule or molecular complex by X-ray diffraction of the crystal;

c) identifying ~~all or part of~~ the structural coordinates of a CnA binding pocket of said molecule or molecular complex of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 150, 151, 156, 160, 199, 232, 253, 254, 256, 281, 282, 283, 284, 306, 311, 312, and 317, which coordinates fall within the range of those recited in Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of 1.5Å and encoding those coordinates on a data storage material ~~said binding pocket~~;

d) utilizing all or part of said structure coordinates defining ~~all or part of~~ said CnA binding pocket and the structure coordinates of one of said plurality of chemical entities to position a chemical entity within all or part of the CnA binding pocket ~~or the CnA homologue binding pocket~~;

e) docking said chemical entity with all or part of the CnA binding pocket ~~or the CnA homologue~~

~~binding pocket~~ by employing computational means which utilize all or part of said structure coordinates ~~of all or part of the~~ defining said CnA binding pocket ~~or~~ and the chemical entity, wherein said docking utilizes energy minimization;

f) analyzing the results of said docking to quantify the association between said chemical entity and all or part of the CnA binding pocket ~~or the CnA homologue binding pocket~~;

g) optionally repeating steps ~~a)~~ d) through ~~e)~~ f) with another of said plurality of chemical entities; and

h) selecting at least one of said plurality of chemical entities that associates with all or part of the CnA binding pocket ~~or the CnA homologue binding pocket~~ based on said quantified association of said chemical entity.

38. (currently amended) A method of using a computer for selecting at least one of a plurality of chemical entities based on its ability to associate with all or part of a molecule or molecular complex comprising a calcineurin A (CnA) binding pocket defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121,

122, 150, 151, 156, 160, 199, 281, 282, 283, 306, 311, 232, and 254 according to Figure 1~~, or a CnA homologue binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å~~; wherein said computer comprises a machine-readable data storage medium comprising a data storage material encoded with said structure coordinates ~~defining all or part of said binding pocket~~ and wherein said method comprises the steps of:

a) producing a crystal of a molecule or molecular complex comprising amino acids [[5-168]] 24-240 and 247-370 of CnA and amino acids [[24-370]] 5-82 and 84-168 of CnB and a chemical entity;

b) determining the three-dimensional structure coordinates of the molecule or molecular complex by X-ray diffraction of the crystal;

c) identifying ~~all or part of~~ a CnA binding pocket of said molecule or molecular complex defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 150, 151, 156, 160, 199, 281, 282, 283, 306, 311, 232, and 254, which coordinates fall within the range of those recited in Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of

1.5Å and encoding those coordinates on a data storage material ~~said binding pocket~~;

d) utilizing all or part of said structure coordinates defining ~~all or part of~~ said CnA binding pocket and the structure coordinates of one of said plurality of chemical entities to position a chemical entity within all or part of the CnA binding pocket ~~or the CnA homologue binding pocket~~;

e) docking said chemical entity with all or part of the CnA binding pocket ~~or the CnA homologue binding pocket~~ by employing computational means which utilize all or part of said structure coordinates ~~of all or part of the~~ defining said CnA binding pocket ~~or~~ and the chemical entity, wherein said docking utilizes energy minimization;

f) analyzing the results of said docking to quantify the association between said chemical entity and all or part of the CnA binding pocket ~~or the CnA homologue binding pocket~~;

g) optionally repeating steps d) through f) with another of said plurality of chemical entities; and

h) selecting at least one of said plurality of chemical entities that associates with all or part of the CnA binding pocket ~~or the CnA homologue binding~~

~~pocket~~ based on said quantified association of said chemical entity.

39. (currently amended) A method of using a computer for selecting at least one of a plurality of chemical entities based on its ability to associate with all or part of a molecule or molecular complex comprising a CnA/CnB binding pocket defined by structure coordinates of CnA amino acids 122, 124, 159, 160, 310, 312, 313, 314, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and calcineurin B (CnB) amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 124, 157, 158, 159, 161, and 162 according to Figure 1~~, or a CnA/CnB homologue binding pocket that has a root mean square deviation from the backbone atoms of said CnA and CnB amino acids of not more than 1.5Å~~;

wherein said computer comprises a machine-readable data storage medium comprising a data storage material encoded with said structure coordinates ~~defining all or part of said binding pocket~~ and wherein said method comprises the steps of:

a) producing a crystal of a molecule or molecular complex comprising amino acids [[5-168]] 24-240

and 247-370 of CnA and amino acids [[24-370]] 5-82 and 84-168 of CnB and a chemical entity;

b) determining the three-dimensional structure coordinates of the molecule or molecular complex by X-ray diffraction of the crystal;

c) identifying ~~all or part of~~ a CnA/CnB binding pocket of said molecule or molecular complex defined by structure coordinates of CnA amino acids 122, 124, 159, 160, 310, 312, 313, 314, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and calcineurin B (CnB) amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 124, 157, 158, 159, 161, and 162, which coordinates fall within the range of those recited in Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of 1.5Å and encoding those coordinates on a data storage material ~~said binding pocket~~;

d) utilizing all or part of said structure coordinates defining ~~all or part of~~ said CnA/CnB binding pocket and the structure coordinates of one of said plurality of chemical entities to position a chemical entity within all or part of the CnA/CnB binding pocket ~~or the CnA homologue binding pocket~~;

e) docking said chemical entity with all or part of the CnA/CnB binding pocket ~~or the CnA homologue~~

~~binding pocket~~ by employing computational means which utilize all or part of said structure coordinates ~~of all or part of the~~ defining said CnA/CnB binding pocket ~~or~~ and the chemical entity, wherein said docking utilizes energy minimization;

f) analyzing the results of said docking to quantify the association between said chemical entity and all or part of the CnA/CnB binding pocket ~~or the CnA/CnB homologue binding pocket~~;

g) optionally repeating steps d) through f) with another of said plurality of chemical entities; and

h) selecting at least one of said plurality of chemical entities that associates with all or part of the CnA/CnB binding pocket ~~or the CnA/CnB homologue binding pocket~~ based on said quantified association of said chemical entity.

40. (currently amended) A method of using a computer for selecting at least one of a plurality of chemical entities based on its ability to associate with all or part of a molecule or molecular complex comprising a CnA/CnB binding pocket defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 124, 150, 151, 156, 159, 160, 199, 232, 253, 254, 256, 281, 282, 283,

284, 306, 310, 311, 312, 313, 314, 317, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and CnB amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 124, 157, 158, 159, 161, and 162 according to Figure 1~~, or a CnA/CnB homologue binding pocket that has a root mean square deviation from the backbone atoms of said CnA and CnB amino acids of not more than 1.5Å~~;

wherein said computer comprises a machine-readable data storage medium comprising a data storage material encoded with said structure coordinates ~~defining all or part of said binding pocket~~ and wherein said method comprises the steps of:

a) producing a crystal of a molecule or molecular complex comprising amino acids [[5-168]] 24-240 and 247-370 of CnA and amino acids [[24-370]] 5-82 and 84-168 of CnB and a chemical entity;

b) determining the three-dimensional structure coordinates of the molecule or molecular complex by X-ray diffraction of the crystal;

c) identifying ~~all or part of~~ a CnA/CnB binding pocket of said molecule or molecular complex defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 124, 150, 151, 156, 159, 160, 199, 232, 253, 254, 256, 281, 282, 283, 284, 306, 310, 311, 312,

313, 314, 317, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and CnB amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 124, 157, 158, 159, 161, and 162, which coordinates fall within the range of those recited in Figure 1 ± a root mean square deviation from the backbone atoms of said amino acids of 1.5 Å and encoding those coordinates on a data storage material ~~said binding pocket~~;

d) utilizing all or part of said structure coordinates defining ~~all or part of~~ said CnA/CnB binding pocket and the structure coordinates of one of said plurality of chemical entities to position a chemical entity within all or part of the CnA/CnB binding pocket ~~or the CnA homologue binding pocket~~;

e) docking said chemical entity with all or part of the CnA/CnB binding pocket ~~or the CnA homologue binding pocket~~ by employing computational means which utilize all or part of said structure coordinates ~~of all or part of the~~ defining said CnA/CnB binding pocket or structure coordinates of the chemical entity, wherein said docking utilizes energy minimization;

f) analyzing the results of said docking to quantify the association between said chemical entity

and all or part of the CnA/CnB binding pocket ~~or the CnA/CnB homologue binding pocket~~;

g) optionally repeating steps d) through f) with another of said plurality of chemical entities; and

h) selecting at least one of said plurality of chemical entities that associates with all or part of the CnA/CnB binding pocket ~~or the CnA/CnB homologue binding pocket~~ based on said quantified association of said chemical entity.

41. (previously presented) The method according to any one of claims 37-40, further comprising the steps of:

i) contacting the selected chemical entity with said molecule or molecular complex; and

j) monitoring the association of the molecule or molecular complex with the selected chemical entity.

42. (previously presented) The method according to any one of claims 37-40, wherein the docking utilizes shape complementarity or is followed by molecular dynamics.

43. (previously presented) The method according to any one of claims 37-40, wherein the docking is

performed through visual inspection on a computer screen using a computer program capable of generating a three-dimensional graphical representation of said structure coordinates and structure coordinates of said chemical entity.

44. (currently amended) The method according to any one of claims 37-40, further comprising the steps of:

i) repeating steps d) to h) with a second set of a plurality of chemical entities that associate with all or another part of the binding pocket ~~or homologue thereof~~;

j) optionally, visually inspecting the relationship of the selected first and second chemical entities to each other in relation to the binding pocket ~~or homologue thereof~~ on a computer screen using the three-dimensional graphical representation of the binding pocket ~~or homologue thereof~~ and said selected first and second chemical entity; and

k) assembling the first and second chemical entities into a compound or complex that associates with all or part of said binding pocket ~~or homologue thereof~~ by model building.

45-56. (cancelled).